REMARKS

The Specification

The Examiner states that the first line of the specification should reflect the status of the priority applications. Applicants have amended the specification to indicate the status of the applications from which this application claims benefit.

The Examiner states that the disclosure is objected to because of informalities regarding recitation of sequence identifiers at page 48 and in the "Brief description of the drawings" section; inconsistencies of labels in the "Brief description of the drawings" section with the labels in the corresponding figures; and extra lines on page 16, lines 5-6 and 10. Applicants have amended the "Brief description of the drawings" section to add sequence identifier, correct the inconsistent labels, and remove the lines on page 16, lines 5-6, and 10.

Regarding the objections to page 48, lines 19 and 21, applicants submit that sequence identifiers were already added to page 48 in their May 25, 1999 Preliminary Amendment. However, applicants note that the Preliminary Amendment recited an incorrect application no. and filing date. Applicants further note that a copy of the Preliminary Amendment was not included in a copy of the file history obtained from the Patent Office, which applicants assume represents the Patent Office's file history. Thus, applicants believe the Preliminary Amendment was never

entered in this application. Accordingly, applicants have amended lines 19 and 21 of page 48 herein to add sequence identifiers. None of the amendments adds new matter.

The Drawings

The Examiner states that the request to amend Drawings filed on November 17, 2000 is acknowledged, but that the Patent and Trademark Office no longer makes drawing changes. The Examiner further states that it is the applicant's responsibility to correct the drawings in accordance with the instructions set forth in PTO-948.

Applicants submit herewith formal drawings of Figures 1 to 86, which address all of the objections set forth in PTO-948. The drawings have additionally been amended to correct the sequence identifiers. None of these amendments adds new matter.

The Claims

Applicants have amended claims 1-4 and 7 to recite that the antibody is an isolated human antibody that specifically binds to human EGF-r. Support for these amendments is found throughout the specification, e.g., at page 44, line 6 to page 98, line 5. Claim 1 also has been amended to add a parenthetical reciting the abbreviation of epidermal growth factor receptor (EGF-r), which is used throughout the claims. Claims 2 and 7 have been amended to correct a minor spelling error. Claim 6 has been amended to correct lack of antecedent basis. None of these amendments adds new matter.

Upon entry of the amendments, claims 1-7 will be pending in the application. Applicants submit that these amendments place the claims in condition for allowance or at least present the rejected claims in better form for consideration on appeal and should therefore be entered after the final rejection. 37 C.F.R. § 1.116(a).

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-7 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly for lack of enablement. The Examiner states that the specification enables the antibody produced by hybridoma E7.6.3. However, the Examiner contends that the specification "does not reasonably provide enablement for antibody that binds to *any* EGFR having the functions mentioned above for treating cancer." The Examiner alleges that the specification discloses "only five humanized antibodies" that bind to human EGF-r, and that only one of these exhibits the properties mentioned above for inhibiting growth of tumor cells expressing EGF-r. In view of the claim amendments, applicants traverse.

Claims 1-7, as amended, are directed to an isolated human antibody wherein said antibody is characterized by one or more of the functions mentioned by the Examiner. For clarification, applicants note that although the Examiner repeatedly refers to the enablement of claims to antibodies for

treating cancer or inhibiting tumor cells or tumors, none of the pending claims include such limitations. The Examiner contends that the specification discloses "only five humanized antibodies" that bind EGF-r. In fact, however, the specification specifically exemplifies twenty-three fully human antibodies that bind EGF-r (E1.1, E2.4, E2.5, E2.11, E6.2, E6.4, E6.3, E7.6.3, E20.1, E20.3, E20.8.1, E20.11.2, E2.18, E20.19.2, E20.21, E20.22, E7.5.2, E7.8.2, E2.6, E7.2, E7.10, E2.5.1, and E2.3.1) (see page 49, line 7 to page 66, line 5; page 68, lines 11 to page 69, line 6; and page 77, lines 13 to 15). Furthermore, the specification provides the nucleotide and amino acid sequences of seventeen of these human anti-EGF-r antibodies (E1.1, E2.4, E2.5, E2.11, E6.2, E6.4, E6.3, E7.6.3, E20.1, E20.3, E20.8.1, E20.11.2, E2.18, E20.19.2, E20.21, E20.22, and E7.5.2) (see figures 1 to 32, 57 to 70 and 72 to 73). Applicants also wish to point out that the exemplified antibodies in this application, which the Examiner referred to as humanized antibodies, are actually fully human antibodies.

The Examiner contends that the specification fails to provide any guidance for making and using any anti-EGF-r antibody having certain recited functional characteristics other than the antibody produced by hybridoma E7.6.3. Applicants disagree. As mentioned above, the application, as filed, teaches how to make human antibodies against EGF-r and the nucleotide and amino acid sequences of seventeen such antibodies (see figures 1 to 32, 57 to 70 and 72 to 73). In

addition, the application, as filed, provides various assays for identifying antibodies with the recited characteristics (page 78, lines 7 to 19; and page 92, line 15 to page 98, line 5). It is routine in the art to screen large numbers of antibodies to identify ones with a desired characteristic using such assays. In view of the teaching in the application, as filed, and routine practice in the art, no undue experimentation is required to make and use the claimed human antibodies. Accordingly, this rejection should be withdrawn.

Claims 1-7 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. The Examiner alleges that "there is insufficient written description about the structure associated with function of any antibody mentioned above for treating any tumor." The Examiner also alleges that "[G]iven the lack of a written description of *any* additional representative species of antibody that have the functional characteristics such as the ones recited in the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus."

Applicants disagree. As noted above, none of the claims contain a limitation to treating tumors. As such, applicants need not teach how to use the antibodies to treat tumors. There is no per se rule as to the number of species of a genus necessary to satisfy the written description requirement. In some instances one example is sufficient. As

described above, applicants have exemplified twenty-three human antibodies that specifically bind EGF-r. EGF-r was, as of the earliest priority date of this application, a well-characterized protein. Furthermore, applicants provided the nucleotide and amino acid sequences of seventeen of the antibodies. Accordingly, this rejection should be withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 6 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner states that "tumor cells" lacks antecedent basis because ECV304 cells are endothelial cells. Applicants have amended claim 6 to correct this inadvertent error, thus obviating this rejection.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-7 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Reins et al., "Anti-epidermal growth factor receptor monoclonal antibodies affecting signal transduction," (1993) *J. Cellular Biochem* 51:236-248 ("Reins"), Defize et al., "Signal transduction by epidermal growth actor occurs through the subclass of high affinity receptors," (1989) *J Cell Biol* 109:2495-507 ("Defize"), Petit et al., "Neutralizing antibodies against epidermal growth factor and ErbB-2/neu receptor tyrosine kinases down-regulate vascular endothelial growth factor production by tumor cells in vitro and in vivo," (1997) Am J Pathol 151:1523-30 ("Petit") or US Patent No. 4,943,533 ("'533 patent"). The Examiner asserts

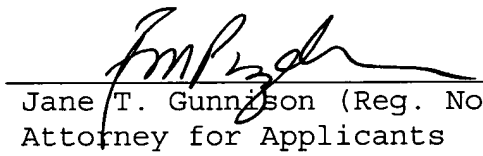
that Reins, Defize, Petit and the '533 patent all teach antibodies that fall within the scope of the claims. Applicants traverse in view of the amendments.

The claims as amended are directed to isolated human antibodies that bind human EGF-r. None of the antibodies taught in Reins, Defize, Petit or the '533 patent teach or suggest such antibodies. Accordingly, these rejections should be withdrawn.

The Examiner is invited to call the attorney of record with any questions or clarification of this submission if needed.

Consideration and allowance of the pending claims is requested.

Respectfully submitted,



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The filing fee has been calculated as shown below:

CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY FILED	PRESENT EXTRA	RATE	ADDITIONAL FEES
TOTAL CLAIMS	- *	=	X $18 =	$ .00
INDEPENDENT CLAIMS	- **	=	X $86 =	$ .00
FIRST PRESENTATION OF A MULTIPLE DEPENDENT CLAIM			+ $290 =	$ .00
			TOTAL	$ .00

* If less than 20, insert 20.
** If less than 3, insert 3.

TOTAL $

[ ] A check in the amount of $____ in payment of the filing fee is transmitted herewith.

[X] The Director is hereby authorized to charge payment of any additional fees required under 37 C.F.R. § 1.16, in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

[ ] Please charge $_____ to Deposit Account No. 06-1075 in payment of the filing fee. A duplicate copy of this transmittal letter is transmitted herewith.

EXTENSION FEE

[X] The following extension is applicable to the Reply filed herewith; [ ] $110.00 extension fee for reply within first month pursuant to 37 C.F.R. § 1.17(a)(1); [ ] $420.00 extension fee for reply within second month pursuant to 37 C.F.R. § 1.17(a)(2); [X] $950.00 extension fee for reply within third month pursuant to 37 C.F.R. § 1.17(a)(3); [ ] $1,480.00 extension fee for reply within fourth month pursuant to 37 C.F.R. § 1.17(a)(4);

[ ] $2,010.00 extension fee for reply within fifth month pursuant to 37 C.F.R. § 1.17(a)(5).

[X] A check in the amount of [ ] $110.00; [ ] 420.00; [X] $950.00; [ ] $1,480.00; [ ] $2,010.00 in payment of the extension fee is transmitted herewith.

[X] The Director is hereby authorized to charge payment of any additional fees required under 37 C.F.R. § 1.17 in connection with the paper(s) transmitted herewith, or to credit any overpayment of same, to Deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

[ ] Please charge the [ ] $110.00; [ ] $420.00; [ ] $950.00; [ ] $1,480.00; [ ] $2,010.00; extension fee to Deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

Respectfully submitted,

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